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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/776,333

02/10/2004

Michael Moshman

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EXAMINER

MERCIER, MELISSA S

ART UNIT

PAPER NUMBER

1615

NOTIFICATION DATE

DELIVERY MODE

02/24/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DLNYDOCKET@BAKERBOTTS.COM

<i>Office Action Summary</i>	Application No. 10/776,333	Applicant(s) MOSHMAN ET AL.	
	Examiner MELISSA S. MERCIER	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2008.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-23 is/are pending in the application.
- 4a) Of the above claim(s) 18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2, 4-17, 20-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Summary

Receipt of Applicants Remarks and Amended Claims filed on November 24, 2008 is acknowledged. Claims 1-2 and 4-23 remain pending in this application. Claims 18-19 remain withdrawn from consideration.

Comments regarding Applicants Statement regarding the March 12, 2008 Interview and the Office Action Dated June 23, 2008.

While it is acknowledged that Applicant did not receive a copy of the Interview Summary dated March 12, 2008, the Examiner believes this matter has already been addressed. Applicants Representatives contacted the Examiner regarding a copy and where informed that the paperwork was sent for scanning, however, it was never scanned into the system. Since the examiner sent the original copy for scanning, no additional copies were available. The Examiner did apologize for the incident and therefore, it is the position of the Examiner that the issue has been adequately addressed.

Withdrawn Objections/Rejections

Specification

The objection to the disclosure because of the following informalities: Applicant has submitted amendments to the specification, which are new matter. Applicant has

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presented amendments, which would change the release profile from first order to zero order kinetics has been withdrawn based on an obvious error.

Claim Rejections - 35 USC § 112

The rejection of claims 1-2, 4-17, 20-23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention with regards to the term “therapeutically effective” and “effective amount” have been withdrawn. Applicant’s amendments to claim 1, in which the morphine is present in an analgesically effective amount and chitosan is present in the amount effective to provide substantially linear absorption rates upon administration is deemed to be definite.

Regarding claim 6, the Examiner has also withdrawn the rejection for “purified morphine”. The Examiner will continue to interpret “purified morphine” to read on any degree of pharmaceutical grade morphine since no purity has been recited.

Claim Rejections - 35 USC § 103

The rejection of claims 1-2, 4-8, 16-17, and 21-23 under 35 U.S.C. 103(a) as being unpatentable over Illum (US Patent 5,629,011) in view of Merck Index Monograph 06276 has been withdrawn. Applicant’s arguments regarding the use of morphine-6-glucuronide and morphine-3-glucuronide are persuasive.

The rejection of claims 1-2, 4-12, 16-17, 20-21, and 23 under 35 U.S.C. 103(a) as being unpatentable over Hansen et al. (US Patent 5,955,502) in view of Merck Index

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Monograph 06276 has been withdrawn. Applicant's arguments regarding the presence of chitosan in oral tablets or capsules and not in the transmucosal formulations are presuasive.

The rejection of claims 1-2, 4-17, and 20-21 under 35 U.S.C. 103(a) as being unpatentable over Dellamary et al. (US Patent 6,433,040) in view of Merck Index Monograph 06276 has been withdrawn. Applicant's arguments regarding the lack of a teaching or motivation as to why one of ordinary skill would select the cited components from the laundry lists of possible components are persuasive.

Newly Applied Rejections/Objections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-17 and 21-23 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the

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claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

While the specification describes chitosan to include chitosan derivatives at p. 5-6, it does not describe how any derivative of chitosan can be employed to in the transmucosal delivery system to convey possession of the entire genus encompassed by chitosan as defined by the specification. Applicant is enabled for chitosan, as the linear polysaccharide composed of randomly distributed β -(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit), not for all derivatives and salts. One of ordinary skill would not expect any and all derivatives and salts of chitosan to have the exact same properties as chitosan.

Claim Rejections - 35 USC § 103

Claims 1-2, 4-17 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum et al. (US Patent 6,387,917).

Illum discloses a methane sulphonate salt of morphine and compositions thereof having medicinal uses, particularly for the treatment of pain and adapted for nasal delivery (abstract). The preferred composition comprises aqueous solutions in which the methane sulphonate salt is combined with chitosan to provide an increased absorption of the drug (column 2, lines 61-68). The morphine methane sulphonate liquid formulation will comprise 0.1mg/mL to about 600mg/mL (column 4, lines 20-24). The

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formulation may also be incorporate into formulations suitable for oral, buccal, rectal, or vaginal administration (column 4, lines 39-42). Illum's Examples 2-3 discloses a solution for intranasal administration comprising 8g morphine base (monohydrate), to which 2M methane sulphonic acid solution is stirred in, and 25mL of chitosan (column 5, line 33 through column 6, line 21). It is noted in claim 9, that Applicant has identified methanesulfonic acid as an antioxidant. Based on the prior art teachings in Example 2 and the instant applications formulations, morphine base monohydrate is not being administered, but rather morphine base, as the methane sulphonate salt. The prior art teaches mixing morphine base monohydrate with methane sulphonic acid in which no additional method steps are performed, (i.e. heating, precipitation), then adding the chitosan solution. Therefore, Applicants is directed to their own specification on page 10-11, in which Applicant has used the same method steps as Illum, and would necessarily result in the conversation of the base monohydrate to the methane sulphonate salt of morphine.

Illum further discloses the formulation can also contain other ingredients such as buffer systems, pH modifiers, anti-oxidants, stabilizing agents, anti-microbial agents, chelating agents, viscosity-enhancing agents, or other agents generally used in pharmaceutical formulations (column 4, lines 25-29).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various transmucosal compositions having various amounts of the active agent and chitosan polymers is within the level of skill of one having ordinary skill in the art at the time of the

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invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See *In re Russell*, 439 F.2d 1228 169 USPQ 426(CCPA 1971).

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues the morphine base monohydrate in Example 2 of Illum is converted to the methane sulphonate salt of morphine upon the addition of 2M methane sulphonic acid. This occurs prior to the addition of the chitosan solution. As recited in the body of the rejection, Applicants specification has also described the same method of preparation as Illum, which would necessarily result in the same product. Applicant is not administered morphine base monohydrate as asserted in the remarks on page 15-16, but rather morphine as a methane sulphonate salt as evidenced by the examples in the instant specification.

Applicant's arguments regarding the Merck Index reference for morphine are persuasive and have therefore been withdrawn as a reference in the rejection. The rejection is over Illum alone.

Conclusion

Due to the new grounds of rejection presented in this office action, this action is made Non-Final. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA S. MERCIER whose telephone

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number is (571)272-9039. The examiner can normally be reached on 8:00am-4:30pm
Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa S Mercier/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615